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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/704,362	11/01/2000	Kalyanaraman Ramnarayan	24737-1906B	4748

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EXAMINER

BRUSCA, JOHN S

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 04/03/2003

49

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/704,362

Applicant(s)

RAMNARAYAN ET AL.

Examiner

John S. Brusca

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 13 February 2003.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 23 and 41-49 is/are pending in the application.
- 4a) Of the above claim(s) 43 and 47 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 23,41,42,44-46,48 and 49 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 01 November 2000 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                              | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>14, 17</u> . | 6) <input type="checkbox"/> Other:  |

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## **DETAILED ACTION**

### ***Election/Restrictions***

1. Newly submitted claims 42, 43, 46, and 47 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: originally filed claim 23 comprises a step that recites "generating 3-D protein structural variant models from the sequences" and that step has been interpreted in the Office action mailed 13 August 2002 to require an ab initio method of determining a protein structure from sequence data of the recited protein. Because the step does not allow for generation of structures from data other than sequence data of the recited protein, some embodiments of claims 42 and 46 drawn to searching protein structure databases or homology modeling are drawn to an invention that is independent or distinct from the invention originally claimed. Claims 43 and 47 are drawn to use of x-ray crystallographic or NMR spectroscopy structural data and are therefore drawn to an invention that is independent or distinct from the invention originally claimed.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 43 and 47 are withdrawn from consideration, and claims 42 and 46 are examined only in part as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

### ***Claim Rejections - 35 USC § 112***

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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Claim 23 and newly filed claims 41, 42, 44-46, 48 and 49 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for reasons of record in the Office action mailed 13 August 2002.

3. Applicant's arguments filed 13 February 2003 have been fully considered but they are not persuasive. The applicants state that the specification shows how to determine the structure of a protein by use of x-ray crystallography, NMR, or a protein structure database, however the elected invention is limited to ab initio methods. The applicants point to example 1 in the instant specification however example 1 utilizes prior art crystal structures of the target NS3 protease of HCV rather than the claimed ab initio determination of protein structure. The applicants point to a number of references in the Information Disclosure Statement filed 13 February 2003. The applicants point to ab initio methods of Belaji et al. (U.S. Patent Nos 5,331,573, 5,579,250, and 5,612,895) as supporting enablement of the elected invention, however Belaji et al. exemplifies ab initio prediction of the structure of endothelin, which is a 21 amino acid peptide, and peptides that bind endothelin. As such, the guidance of Belaji et al. is not commensurate with the scope of the claimed invention which requires ab initio prediction of proteins. The applicants point to ab initio methods of Osguthorpe. Osguthorpe shows some success at prediction of secondary structure, however Osguthorpe further points out on page 192:

However, these results also show how even with secondary structure predictions of 60-70%, generating correct tertiary structures requires significant additional information as the overall RMS of these structures ranges from 10 to 19 (excluding T0065).

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The applicants point to Westhead and Thornton for support of enablement, however on page 387 they summarize by saying that the quality of models is dependent on comparison to sequences of related sequences with known structures, and that when less than 20% of the sequence of interest is similar to a known structure the modeling algorithms rapidly deteriorate and the inaccuracies are very large. The applicants point to Jones for support of enablement, however Jones summarizes on page 190 that "the predicted structure was quite a long way from the experimental structure." The applicants point to Samudrala et al. for support of enablement, however Samudrala et al. points out in the abstract that less than half of the proteins analyzed had a predictable structure, and Table 1 shows that the level of resolution of the predictions was low. The applicants argue that Koehl et al. does not show poor performance of ab initio methods, however it is maintained that figure 2 of Sternberg et al. and Table 1 of Koehl et al. show poor performance when no structural data is available. The applicants further argue that accurate predictions of structure are not required to use the method, however because the method requires prediction of clinical results after comparison of a reference target protein and a variant protein of a patient, it is not clear how such a comparison can be made if the predicted structures are inaccurate.

4. The rejection of claim 23 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention in the Office action mailed 13 August 2002 is withdrawn in view of the amendment filed 13 February 2003.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 42 and 46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 42 and 46 are indefinite for recitation of the phrase "experimental methods" in line 3 of claim 42 and line 3 of claim 46 because it is not clear if the claim is limited to the elected invention which uses ab initio methods of structure determination from sequence data. The rejection would be overcome by deletion of the phrase from claims 42 and 46.

Claims 42 and 46 are indefinite for recitation of the phrase "searching protein structure databases, homology modeling" because the limitations are not drawn to the elected invention. The rejection would be overcome by deletion of the phrase from claims 42 and 46.

### ***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

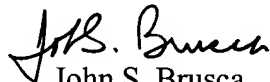
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to John S. Brusca whose telephone number is 703 308-4231. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on 703 308-4025. The fax phone numbers for the organization where this application or proceeding is assigned are 703 746-5137 for regular communications and 703 746-5137 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308-0196.



John S. Brusca  
Primary Examiner  
Art Unit 1631

jsb  
April 2, 2003